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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/972,916	10/10/2001	Peter M. Thule	US 1292/01 (VA)	4645

7590 03/20/2007

Law Office - Dinesh Agarwal, P.C.
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EXAMINER	
ANGELL, JON E	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/972,916	THULE, PETER M.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 17-21* is/are pending in the application.

4a) Of the above claim(s) *17-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 3/14/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 3/14/2006.

1. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Status if the Claims

Claims 1-15 and 17-21 are currently pending.

Claims 17-21 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/21/2004.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Thule et al (Diabetes May 1999, supplement— previously cited) as evidenced by Thule and Liu presentation at the ADA 59th Annual Meeting, June 1999 (provided as Reference 3 in the

IDS filed 3/14/2006) and Vaulont et al. (J. Mol. Biol. 1989, Vol. 209, pages 205-219) and Goswami et al. (Endocrinology 1994, Vol. 134, pages 736-743).

The instant claims are drawn to an insulin regulator construct comprising a nucleotide sequence as set forth in any one of SEQ ID NOS: 3-6 (each of which comprises a GIRE of the L-PK gene promoter and an insulin sensitive element of the IGFBP-1 basal promoter) and a sequence encoding insulin or proinsulin operably linked to the promoter element of the construct (e.g., see claim, 1 and 9); wherein the GIRE comprises an HNF-4 binding site and a glucose responsive site (claim 2); wherein the construct comprises a plurality of GIREs (claim 3); wherein the HNF-4 binding site and the GIRE are in a native orientation (claim 4); wherein the HNF-4 binding site and the GIRE are reversed from a native orientation (claim 5); wherein the GIRE is upstream of the insulin sensitive element (claim 6); wherein the GIRE comprises a nucleotide sequence as set forth in SEQ ID NO: 1 (claim 7); wherein the insulin sensitive element comprises a nucleotide sequence as set forth in SEQ ID NO: 2 (claim 8); wherein the construct is not stimulated by lactate or sucrose (claim 10); wherein glucose stimulates expression of the construct and wherein insulin inhibits expression the construct (claim 11); wherein the construct is comprised in a vector (claim 12); wherein the vector is an adenoviral vector (claim 13); wherein the construct comprises a transgene (claim 14); and wherein the construct is comprised in a pharmaceutical composition with a pharmaceutically acceptable carrier or diluent (claim 15).

It is noted that the specification describes a construct comprising all of the elements in an adenoviral vector and names the vector Ad/$(GIRE)_3$BP-1 2xfur (which is

an adenoviral vector comprising 3 GIREs, the insulin sensitive element of IGFBP-1 operably linked to a sequence encoding a proinsulin molecule).

Thule (Diabetes) is an abstract from a presentation that the inventor gave more than one year before the effective filing date of the instant application. The abstract teaches an adenoviral vector which is described as comprising all of the claimed elements, and which also named Ad/$(GIRE)_3$BP-1 2xfur. Since the Ad/$(GIRE)_3$BP-1 2xfur vector taught by the Thule (Diabetes) abstract appears to be the same vector described in the specification, it must, by necessity meet all of the limitations of the claims. Furthermore, in the presentation given by the Inventor at the ADA 59th Annual Meeting June 1999, which is the presentation associated with the Thule (Diabetes) abstract, the slides (e.g., see slides 2 and 3) clearly describe the elements used to construct the Ad/$(GIRE)_3$BP-1 2xfur vector. Specifically, the slides indicate the exact nucleotides of the rL-PK (nucleotides –125 to –173) and rIGFBP-1 (nucleotides –111 to +96) promoter elements used to construct the vector. Furthermore the nucleotide sequences of the rL-PK and rIGFBP-1 promoter elements were known in the art, as evidenced by Vaulont et al (see Figure 9 which discloses nucleotides –125 to -173 of rL-PK) and Goswami et al (See Figure 3A which discloses nucleotides –111 to +96 of rIGFBP-1). Therefore, the Thule abstract, as evidenced by the Thule presentation and as further evidenced by Vaulont et al and Goswami et al, provides an enabling disclosure which teaches the claimed invention. Accordingly, the instant claimed invention was described in a printed publication in this country more than one year prior to the date of application for patent in the United States.

Claims 1-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Thule et al (Abstract from meeting June 9-13, 1999, previously cited) as evidenced by Thule and Liu presentation at the American Society of Gene Therapy 2nd Annual Meeting, June 1999 (provided as Reference 4 in the IDS filed 3/14/2006) and Vaulont et al. (J. Mol. Biol. 1989, Vol. 209, pages 205-219) and Goswami et al. (Endocrinology 1994, Vol. 134, pages 736-743).

The instant claims are drawn to an insulin regulator construct comprising a nucleotide sequence as set forth in any one of SEQ ID NOS: 3-6 (each of which comprises a GIRE of the L-PK gene promoter and an insulin sensitive element of the IGFBP-1 basal promoter) and a sequence encoding insulin or proinsulin operably linked to the promoter element of the construct (e.g., see claim, 1 and 9); wherein the GIRE comprises an HNF-4 binding site and a glucose responsive site (claim 2); wherein the construct comprises a plurality of GIREs (claim 3); wherein the HNF-4 binding site and the GIRE are in a native orientation (claim 4); wherein the HNF-4 binding site and the GIRE are reversed from a native orientation (claim 5); wherein the GIRE is upstream of the insulin sensitive element (claim 6); wherein the GIRE comprises a nucleotide sequence as set forth in SEQ ID NO: 1 (claim 7); wherein the insulin sensitive element comprises a nucleotide sequence as set forth in SEQ ID NO: 2 (claim 8); wherein the construct is not stimulated by lactate or sucrose (claim 10); wherein glucose stimulates expression of the construct and wherein insulin inhibits expression the construct (claim 11); wherein the construct is comprised in a vector (claim 12); wherein the vector is an adenoviral vector (claim 13); wherein the construct comprises a transgene (claim 14); and

wherein the construct is comprised in a pharmaceutical composition with a pharmaceutically acceptable carrier or diluent (claim 15).

It is noted that the specification describes a construct comprising all of the elements in an adenoviral vector and names the vector Ad/$(GIRE)_3$BP-1 2xfur (which is an adenoviral vector comprising 3 GIREs, the insulin sensitive element of IGFBP-1 operably linked to a sequence encoding a proinsulin molecule).

The Thule abstract is an abstract from a presentation that the inventor gave more than one year before the effective filing date of the instant application. The abstract teaches an adenoviral vector which is described as comprising all of the claimed elements, and which also named Ad/$(GIRE)_3$BP-1 2xfur. Since the Ad/$(GIRE)_3$BP-1 2xfur vector taught by Thule appears to be the same vector described in the specification, it must, by necessity meet all of the limitations of the claims. Furthermore, in the presentation given by the Inventor at the American Society of Gene Therapy 2nd Annual Meeting June 1999, which is the presentation associated with the Thule abstract, the slides (e.g., see slides 3 and 4) clearly describe the elements used to construct the Ad/$(GIRE)_3$BP-1 2xfur vector. Specifically, the slides indicate the exact nucleotides of the rL-PK (nucleotides –125 to –173) and rIGFBP-1 (nucleotides –111 to +96) promoter elements used to construct the vector. Furthermore the nucleotide sequences of the rL-PK and rIGFBP-1 promoter elements were known in the art, as evidenced by Vaulont et al (see Figure 9 which discloses nucleotides –125 to -173 of rL-PK) and Goswami et al (See Figure 3A which discloses nucleotides –111 to +96 of rIGFBP-1). Therefore, the Thule abstract, as evidenced by the Thule presentation and as further evidenced by Vaulont et al and Goswami et al, provides an enabling disclosure which teaches the

claimed invention. Accordingly, the instant claimed invention was described in a printed publication in this country more than one year prior to the date of application for patent in the United States.

Claims 1-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Thule et al (Abstract from meeting of June 1998—previously cited) as evidenced by Thule and Liu presentation at the ADA 58th Annual Meeting, June 1998 (provided as Reference 2 in the IDS filed 3/14/2006) and Vaulont et al. (J. Mol. Biol. 1989, Vol. 209, pages 205-219) and Goswami et al. (Endocrinology 1994, Vol. 134, pages 736-743).

The instant claims are drawn to an insulin regulator construct comprising a nucleotide sequence as set forth in any one of SEQ ID NOS: 3-6 (each of which comprises a GIRE of the L-PK gene promoter and an insulin sensitive element of the IGFBP-1 basal promoter) and a sequence encoding insulin or proinsulin operably linked to the promoter element of the construct (e.g., see claim, 1 and 9); wherein the GIRE comprises an HNF-4 binding site and a glucose responsive site (claim 2); wherein the construct comprises a plurality of GIREs (claim 3); wherein the HNF-4 binding site and the GIRE are in a native orientation (claim 4); wherein the HNF-4 binding site and the GIRE are reversed from a native orientation (claim 5); wherein the GIRE is upstream of the insulin sensitive element (claim 6); wherein the GIRE comprises a nucleotide sequence as set forth in SEQ ID NO: 1 (claim 7); wherein the insulin sensitive element comprises a nucleotide sequence as set forth in SEQ ID NO: 2 (claim 8); wherein the construct is not stimulated by lactate or sucrose (claim 10); wherein glucose stimulates expression of the construct and wherein insulin inhibits expression the construct (claim

11); wherein the construct is comprised in a vector (claim 12); wherein the vector is an adenoviral vector (claim 13); wherein the construct comprises a transgene (claim 14); and wherein the construct is comprised in a pharmaceutical composition with a pharmaceutically acceptable carrier or diluent (claim 15).

It is noted that the specification describes a construct comprising all of the elements in an adenoviral vector and names the vector Ad/$(GIRE)_3$BP-1 2xfur (which is an adenoviral vector comprising 3 GIREs, the insulin sensitive element of IGFBP-1 operably linked to a sequence encoding a proinsulin molecule).

The Thule abstract is an abstract from a presentation that the inventor gave more than one year before the effective filing date of the instant application. The abstract teaches an adenoviral vector which is described as comprising all of the claimed elements, and which also named Ad/$(GIRE)_3$BP-1 2xfur. Since the Ad/$(GIRE)_3$BP-1 2xfur vector taught by the Thule abstract appears to be the same vector described in the specification, it must, by necessity meet all of the limitations of the claims. Furthermore, in the presentation given by the Inventor at the ADA 58th Annual Meeting June 1998, which is the presentation associated with the Thule abstract, the slides (e.g., see slides 3, 4 and 14) clearly describe the elements used to construct the Ad/$(GIRE)_3$BP-1 2xfur vector. Specifically, the slides indicate the exact nucleotides of the rL-PK (nucleotides –125 to –173) and rIGFBP-1 (nucleotides –111 to +96) promoter elements used to construct the vector. Furthermore the nucleotide sequences of the rL-PK and rIGFBP-1 promoter elements were known in the art, as evidenced by Vaulont et al (see Figure 9 which discloses nucleotides –125 to -173 of rL-PK) and Goswami et al (See Figure 3A which discloses nucleotides –111 to +96 of rIGFBP-1). Therefore, the Thule abstract, as

evidenced by the Thule presentation and as further evidenced by Vaulont et al and Goswami et al, provides an enabling disclosure which teaches the claimed invention. Accordingly, the instant claimed invention was described in a printed publication in this country more than one year prior to the date of application for patent in the United States.

Response to Arguments

Applicants submission of the references of the 3/14/2006 IDS is a proper response to the Request for Information under 37 CFR 1.105.

Applicant's arguments filed 8/18/2005 have been fully considered but they are not persuasive.

Applicants argue that independent claim 9 is directed to a construct comprising SEQ ID Nos: 3-6. Applicants assert that none of the Thule abstracts cited disclose the sequences of claim 9. Applicants contend that the Examiner has used the Applicants own disclosure against him in rejecting the claims. Applicants also argue that the Examiner has not shown how one of ordinary skill in the art would arrive at the specifically claimed sequences, absent the Applicants own disclosure.

In response, it is acknowledged that the Thule abstracts do explicitly disclose the sequences of claim 9. However, considering the information which applicants have provided in the 3/14/2006 IDS, it is clear that the presentations given by the Inventor, which are the presentations associated with the cited abstracts, disclosed sufficient information which allow one of ordinary skill art to construct the claimed vector. Specifically, the presentations disclosed the exact regions of nucleotide sequences used to construct the elements which are the sequences of claim 9. Furthermore, as evidenced by

Vaulont et al. and Goswami et al. the exact nucleotide sequences disclosed by Thule could be constructed without knowledge of the Applicant's disclosure. Therefore, Applicants arguments are not persuasive.

Conclusion

Since the instant rejections rely on evidence presented in response to an Information Request under 37 CFR 1.105, the instant Action is made non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on 9:00 a.m.- 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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